REMARKS

This amendment was originally submitted on August 13, 2010. Applicants received an Advisory Action dated September 2, 2010 stating the amendment will not be entered because it raises new issues. Applicants are re-submitting the amendment along with a Request for Continued Examination.

Claims 29-37, 48 and 49 are pending in this application. Support for the amendment to claim 29 can be found, for example, in the final paragraph on page 15 of the specification. No new matter has been introduced into the application through this amendment.

Applicants note with appreciation that the previous rejections under 35 U.S.C. § 102 have been withdrawn in view of the amendments and arguments presented in the response Applicants' filed in October, 2009.

Claims 30-31 remain rejected under 35 U.S.C. §103 as unpatentable over Suhner, *Aviation, Space Env. Med.* 72:638-646 (2001), in view of Ohkawa, U.S. Patent 6,348,485, and the rejection now has been extended to also cover claims 34-37, 48 and 49. The examiner asserted that the Suhner reference discloses that the combination of melatonin and zolpidem can reduce sleep latency/promote sleep initiation to a greater degree than either compound alone. Ohkawa was cited as teaching the administration of a melatonin agonist and zolpidem in a single pharmaceutical formulation form or as separate dosage forms. this rejection is traversed.

The Suhner reference focuses on efforts to reduce jet-lag in eastward-flying trans-Atlantic travelers. Subjects in the study were administered zolpidem, melatonin or a combination thereof on a transatlantic flight and then once daily at bedtime for 4 consecutive days post-flight. The subjects self-rated a number of factors, including total sleep time, sleep latency, overall sleep quality, ease of falling asleep, ease of getting up and quality of morning wakefulness.

The authors report that zolpidem treatment alone was rated the *most effective jet lag medication*. The authors stated that total sleep time was longest in subjects taking zolpidem alone and their sleep latency was the shortest of any group. They also asserted that the subjects taking zolpidem alone *felt more rested in the morning* compared with the other groups. Significantly, they found that the *subjects taking a combination of zolpidem and melatonin found it more difficult to wake up and become fully alert in the mornings* as compared with the other groups.

These teachings are in direct contrast to the present invention. Applicants have found that when sustained release melatonin is administered to a person in combination with a non-benzodiazepine, non-barbiturate compound, such as zolpidem, the melatonin can both potentiate the compound's hypnotic effect and enhance the person's vigilance the next day. Independent claim 29 has been amended above to specifically recite both of these advantages. One of skill in the art reading the Suhner paper would not have any reason to believe that the administration of a hypnotic compound and sustained release melatonin could have such effects.

Claims 32 and 33 remain rejected under 35 U.S.C. §103(a) as unpatentable over Suhner in view of Ohkawa, as applied to claims 30 and 31 above, taken further in view of Richardson, U.S. Patent 6,042,849. The examiner relied upon the primary and secondary references as she had in the preceding rejection. The tertiary reference was cited as teaching a dual layer tablet which has an immediate release layer and a controlled release layer. The examiner asserted that it would have been obvious to use the drug combination taught by Suhner in the dual layer tablet taught by Richardson. This rejection is traversed.

The deficiencies of the Suhner and Ohkawa references have been discussed above, and that discussion is equally applicable to the present rejection. The teachings of the tertiary Richardson reference do not compensate for the shortcomings of the primary and secondary references. The cited references, whether alone or in combination, do not suggest the administration of melatonin and a non-benzodiazepine hypnotic to promote sleep initiation for a person who has difficulty falling asleep, wherein the melatonin is administered in an amount effective both to potentiate the non-benzodiazepine compound's hypnotic effect and to enhance daytime vigilance.

Claims 29-31 and 34-37 remain rejected under 35 U.S.C. § 103(a) as unpatentable over the Ohkawa reference, and the rejection now has been extended to claims 48 and 49 as well. The examiner asserted that the reference teaches administering a melatonin agonist in combination with another drug, such as zolpidem, to treat sleep disorders, including primary insomnia. This rejection is traversed.

As Applicants have noted above, one of skill in the art reading the complete Ohkawa reference, including the Experimental Example bridging columns 9 and 10 would come away believing that the combination of one particular melatonin agonist and one of four specific selected benzodiazepine and non-benzodiazepine compounds taught by Ohkawa would have an impact on sleep disorders only by affecting the latencies of stage 3 and stage 4 sleep. This is very different from Applicants' discovery that the administration of melatonin and a non-benzodiazepine hypnotic drug can promote both sleep initiation in a human who has difficulty falling asleep and the person's daytime vigilance. Based on the teachings of the Ohkawa's example, one of skill in the art would interpret Ohkawa's reference to treating sleep disorders as meaning that sleep quality could be affected, not that sleep initiation could be affected, and there is nothing in the reference to suggest that daytime vigilance actually can be improved.

Claims 32 and 33 remain rejected under 35 U.S.C. § 103(a) as unpatentable over Ohkawa in view of Richardson. The Ohkawa reference was applied as in the previous rejection, and Richardson was cited as in the rejection above of claims 32 and 33. This rejection is traversed.

The deficiencies of the Ohkawa reference have been discussed at length above, and that discussion is equally applicable to the present rejection. The teachings of the Richardson patent do not compensate for the shortcomings of Ohkawa. There is nothing in either reference, taken together or independently that suggests that melatonin and a non-benzodiazepine hypnotic can be administered to promote both sleep initiation and daytime vigilance.

Applicants respectfully submit that the pending claims as amended are patentable over the cited references.

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